REMARKS

Amendments to the Claims

Claim 23 has been amended to recite "consisting essentially of an amino acid sequence selected from the group consisting of SEQ ID NO:1, SEQ ID NO:5 and SEQ ID NO:23." Support for this recitation is found, for example, in Claims 27, 28, 30 and 31 as originally filed. Additional support is found, for example, at page 18, lines 3-11 and at page 25, lines 10-18.

The amended claims are supported by the subject application as originally filed. Therefore, this Amendment adds no new matter.

Additional remarks are set forth below with reference to the numbered paragraphs in the Office Action.

Paragraph 2. Reconsideration of Species Election

Applicant thanks the Examiner for extending the search to cover SEQ ID NO:5, SEQ ID NO:23 and the condition of sepsis.

Paragraph 6. Rejection of Claims 23-42 Under 35 U.S.C. § 112, Second Paragraph

The Examiner has rejected Claims 23-42 under 35 U.S.C. § 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. In the Examiner's opinion, Claim 23 contains the trademark/trade name etanercept, and as such does not identify the goods associated with the trademark or trade name, making the description indefinite. Applicant respectfully disagrees with the Examiner regarding the status of the name etanercept. Although etanercept does describe a recombinant human soluble TNFα receptor, the term is recognized as a generic name (See, for example, Physicians' Desk Reference, 60 Edition, page 580 (2006)). Accordingly, the use of the term etanercept in Claim 23 is not indefinite.

Reconsideration and withdrawal of this rejection are requested.

Paragraph 8. Rejection of Claim 37 Under 35 U.S.C. § 112, First Paragraph

The Examiner has rejected Claim 37 under 35 U.S.C. § 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor, at the time the application was filed, had possession of the claimed invention. In the Examiner's opinion, the phrase "human antibody" in Claim 37 represents a departure from the specification and the claims as originally filed. Applicant's Amendment filed March 30, 2006 pointed to page 30, lines 4-9 for support of the newly added limitation "human antibody" in Claim 37. The Examiner asserts that the specification on page 30, lines 4-9 is limited in scope to only a human antibody obtained by phage display technology, while Claim 37 generically states any human antibodies.

Applicant respectfully disagrees with the Examiner. The specification provides for antibodies against vertebrate HMGB, mammalian HMGB1 and human HMGB1 polypeptides. The written description requirement is satisfied where the specification describes the claimed invention in sufficient detail so that one skilled in the art can reasonably conclude that the inventor had possession of the claimed invention. Vas-Cath, Inc. v Mahurkar, 19 U.S.P.Q.2d 1111 (Fed. Cir. 1991). Moreover, a patent need not teach, and preferably omits, that which is well known in the art. Hybritech, Inc. v. Monoclonal Antibodies, Inc., 231 U.S.P.Q. 81, 94 (Fed. Cir. 1986), cert. denied, 480 U.S. 947 (1987). The analysis of whether the specification complies with the written description requirement is conducted from the standpoint of one of skill in the art at the time the application was filed (Wang Labs v. Toshiba Corp., 26 U.S.P.Q.2d 1767, 1774 (Fed. Cir. 1993)), and should include a determination of the field of the invention and the level of skill and knowledge in the art. M.P.E.P. § 2163, p. 2100-178 (8th Ed., Latest Rev., August 2005). Various techniques for generating human antibodies were well known in the art at the time of the invention (see, for example, U.S. Patent Application 10/147,447, Tracey, *et al.*, incorporated by reference in the specification as filed). Such techniques included, for example, methods for generating transgenic animals capable of producing a repertoire of human antibodies (see, e.g., Jakobvits et al. (Proc. Natl. Acad. Sci. USA, 90: 2551-2555 (1993) and Jakobvits et al. (Nature, 362: 255-258 (1993)); of record, cited as Reference Nos. C77 and C78 respectively) and methods for generating human monoclonal antibodies (see, e.g., Ohlin et al. (Immunology 68:325-331 (1989)) and Sjögren-Jansson et al. (Hybridoma 10(3):411-419 (1991); of record, cited as Reference Nos. C79 and C80, respectively). Accordingly, in view of the teachings in the

specification and the skill and knowledge in the art at the time of the invention, the instant specification provides sufficient written description for the claimed human antibodies. Reconsideration and withdrawal of the rejection are respectfully requested.

Paragraph 9. Rejection of Claims 23-26, 29 and 32-42 Under 35 U.S.C. § 112, First Paragraph

The Examiner has rejected Claims 23-26, 29 and 32-42 under 35 U.S.C. § 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor, at the time the application was filed, had possession of the claimed invention. The Examiner concedes that Applicant was in possession of a method of treating a condition in a patient characterized by activation of an inflammatory cytokine cascade comprising administering to said patient a composition comprising an antibody that binds to HMGB1 polypeptide consisting of SEQ ID NO: 1, 5 or 23 and an agent that inhibits TNF biological activity, wherein said agent is selected from the group consisting of infliximab, etanercept, adalimumab, CDP870, CP571, lenercept and thalidomide (Office Action, page 3). However, the Examiner asserts that Applicant was not in possession of the following:

> a method of treating a condition in a patient characterized by activation of an inflammatory cytokine cascade comprising administering to said patient a composition comprising an antibody that binds to any HMGB polypeptide or a biologically active fragment thereof and an agent that inhibits TNF biological activity, wherein said agent is selected from the group consisting of infliximab, etanercept, adalimumab, CDP870, CP571, Lenercept and Thalidomide as claimed in Claim 23;
>
> a method wherein the HMGB polypeptide is a mammalian peptide, as claimed in Claim 25; and
>
> a method wherein the HMGB polypeptide is any HMGB1 polypeptide, as claimed in Claim 26.

The Examiner states that Applicant has disclosed SEQ ID NO: 1, 5 and 23, and that the skilled artisan cannot envision all of the contemplated HMGB sequence possibilities recited in the instant claims (Office Action, page 4). Accordingly, in the Examiner's opinion, the

specification fails to demonstrate that Applicants had possession of the invention as claimed. While not agreeing with the Examiner, independent Claim 23 has been amended to recite "consisting essentially of an amino acid sequence selected from the group consisting of SEQ ID NO:1, SEQ ID NO:5, and SEQ ID NO:23", in order to expedite prosecution. Reconsideration and withdrawal of the rejection are respectfully requested.

Paragraph 11. Rejection of Claims 23-42 Under 35 U.S.C. § 103(a)

The Examiner has rejected Claims 23-42 under 35 U.S.C. § 103(a) as being unpatentable over U.S. Patent No. 6,468,533 (Tracey *et al.*, hereinafter the '533 Patent) in view of U.S. Patent No. 6,677,321 (Levin, hereinafter the '321 Patent).

The Examiner asserts that the '533 Patent teaches a method of treating rheumatoid arthritis and sepsis, which are characterized by activation of an inflammatory cytokine cascade comprising administering to a patient a composition comprising an antibody that binds to an HMGB polypeptide or a biologically active fragment thereof and an agent such as TNF, wherein the composition further comprises a pharmaceutically acceptable carrier (Office Action, pages 4-5). The Examiner further asserts that the '533 Patent teaches that it has become apparent that a large, highly diverse group of proteins including several transcription factors and other DNA-interacting proteins, contain one or more regions similar to HMG1, and this feature has come to be known as the HMG1 box or HMG1 domain (Office Action, page 5).

The Examiner also asserts that the '533 Patent teaches monoclonal, humanized and human antibodies against native or recombinant HMG1 or fragments thereof, and further teaches a pharmaceutical composition comprising an antagonist or inhibitor of HMG1, wherein the antagonist is antibodies that bind to an HMG1 protein, to treat conditions mediated by the inflammatory cytokine cascade. The Examiner further asserts that the '533 Patent teaches neutralizing antibodies against HMG1 are preferred for therapeutic applications, and that a composition comprising an antibody that specifically binds an HMG1 protein, wherein the antibody inhibits HMG1-mediated activation of the inflammatory cytokine cascade caused inflammation such as sepsis. The Examiner also asserts that the '533 Patent teaches that treatment with anti-HMG1 antibodies provided full protection from LD_{100} doses of LPS in mice, HMG1 is inducible by TNF and IL-α, and dose-dependently stimulates TNF release from

huPBMCs, TNF is a marker of macrophage activation, and that TNF stimulates the release of HMG1 from murine macrophage RAW 264.7 cells. Accordingly, the Examiner concludes that antibodies to HMG1 that neutralize or antagonize the biological activity of HMG1 would inhibit the release of TNF from the macrophage cells.

In the Examiner's opinion, the claimed invention differs from the teachings of the '533 Patent only by the recitation that the agent is infliximab or etanercept in Claim 23 (Office Action, page 5).

The Examiner asserts that the '321 Patent teaches that treatment with a chimeric monoclonal antibody to TNF-α has been shown to suppress inflammation and improve patient well-being in rheumatoid arthritis. The Examiner further asserts that the '321 Patent teaches that infliximab and etanercept have been shown to be effective for short-term treatment of rheumatoid arthritis (Office Action, pages 5-6).

The Examiner asserts that it would have been obvious to one of ordinary skill in the art at the time the invention was made to substitute the TNF or anti-TNF antibody taught by the '533 Patent with the infliximab or etanercept taught by the '321 patent in a method of treating a condition in a patient characterized by activation of an inflammatory cytokine cascade. According to the Examiner, the person of ordinary skill in the art at the time the invention was made would have been motivated to substitute the TNF or anti-TNF antibody with the infliximab or etanercept because such TNF inhibitors were shown to be effective for short-term treatment of inflammation, such as rheumatoid arthritis, as taught by the '321 Patent. The Examiner further asserts that from the combined teachings of the references, the person of ordinary skill in the art would have had a reasonable expectation of success in producing the claimed invention (Office Action, page 6).

Applicant respectfully disagrees. To establish prima facie obviousness, the prior art must teach or suggest all of the claim limitations. In re Royka, 180 U.S.P.Q. 580 (C.C.P.A. 1974). In addition, a finding that the claimed invention is obvious under 35 U.S.C. § 103 requires that (1) "the prior art would have suggested to those of ordinary skill in the art that they should make the claimed composition or device, or carry out the claimed process;" and (2) that "the prior art would also have revealed that in so making or carrying out, those of ordinary skill would have a reasonable expectation of success." In re Vaeck, 20 U.S.P.Q.2d 1438, 1442 (Fed. Cir. 1991).

"Both the suggestion and the reasonable expectation of success must be founded in the prior art, not in the applicant's disclosure." Id. (emphasis added). Moreover, when determining patentability under 35 U.S.C. § 103, the prior art must be considered as a whole, including portions that would lead away from the claimed invention. W.L. Gore & Associates, Inc. v. Garlock, Inc., 721 F.2d 1540, 220 U.S.P.Q. 303 (Fed. Cir. 1983), cert. denied, 469 U.S. 851 (1984).

The Examiner asserts that the claimed invention differs from the '533 Patent by the recitation that the agent is infliximab or etanercept (Office Action, page 5). The Examiner is of the opinion, however, that the addition of the teachings of the '321 Patent would provide one of ordinary skill in the art with the requisite suggestion and reasonable expectation of success needed to establish prima facie obviousness. This is simply not the case. In order to establish prima facie obviousness, the prior art must teach or suggest the claimed invention and provide a reasonable expectation of success. In contrast to the Examiner's assertion, the cited references do not provide the requisite suggestion and reasonable expectation of success required to establish prima facie obviousness.

The '321 Patent teaches the use of cetyl myristoleate (CMO) and CMO compounds in combination with other compounds useful for treating inflammatory disease. Unlike Applicant's specification, the '321 Patent is not even directed towards HMG or its involvement in proinflammatory cytokine release. Instead the '321 Patent focuses on the use of chemical compounds, not antibodies, for the treatment of inflammatory disease. It does not provide any suggestion of combining a TNF antagonist, such as infliximab or etanercept, with an antibody that binds to an HMGB polypeptide to treat inflammatory disease. In the absence of such teachings, the person of ordinary skill in the art would not have been motivated to treat a condition in a patient characterized by activation of an inflammatory cytokine cascade which comprises administering to a patient a composition comprising an antibody that can bind to an HMGB polypeptide consisting essentially of an amino acid sequence selected from the group consisting of SEQ ID NO:1, SEQ ID NO:5, and SEQ ID NO:23 and an agent that inhibits TNF biological activity, selected from the group consisting of infliximab, etanercept, adalimumab, CDP870, CDP571, lenercept, and thalidomide.

Thus, the cited references fail to provide the suggestion and reasonable expectation of success, which are required to establish prima facie obviousness. Accordingly, reconsideration and withdrawal of the rejection are respectfully requested.

Paragraph 12. Rejection of Claims 23-42 Under 35 U.S.C. § 103(a)

The Examiner has rejected Claims 23-42 under 35 U.S.C. § 103(a) as being unpatentable over U.S. Patent Application Publication 2003/0060410 (Tracey *et al.*, hereinafter the '410 Publication) in view of the '321 Patent.

The Examiner asserts that the '410 Publication teaches and claims a method of treating a condition in a patient characterized by activation of an inflammatory cytokine cascade, comprising administering to the patient a purified preparation of antibodies that specifically bind to a vertebrate high mobility group protein (HMG) B box but does not specifically bind to non-B-box epitopes of HMG, in an amount sufficient to inhibit the inflammatory cytokine cascade. The Examiner further asserts that the '410 Publication teaches that the composition can inhibit a condition characterized by activation of an inflammatory cytokine cascade. The Examiner also asserts that the '410 Publication teaches that the composition can further comprise an antagonist or an early sepsis mediator and that it is preferably an antagonist of a cytokine such as TNF, more preferably an antibody to TNF receptor antagonist, wherein the condition is sepsis or rheumatoid arthritis.

According to the Examiner, the '410 Publication teaches that the antibodies can inhibit a biological activity of an HMG B box polypeptide, for example, the release of a proinflammatory cytokine from a vertebrate cell treated with HMG. The Examiner further asserts that the '410 Publication teaches that the HMG B box is a mammalian HMG B box, a human HMG B box, an HMG1 B box, an HMG1 B box with the amino acid sequence of SEQ ID NO:5 or SEQ ID NO:20, and that the antibodies bind a specific polypeptide sequence of the HMG1 B box, comprising amino acids 1-20 of SEQ ID NO:5, or consisting of amino acids 1-20 of SEQ ID NO:20, or consisting of amino acids 1-20 of SEQ ID NO:5. The Examiner asserts that the '410 Publication also teaches that "antibodies" include monoclonal, polyclonal, chimeric, single chain, simianized and humanized antibodies, as well as Fab fragments, including the products of an Fab immunoglobulin expression library. In addition, the Examiner asserts that the '410

Publication teaches phage display technology and can be utilized to select antibody genes with binding activities towards the polypeptide either from repertoires of PCR amplified v-genes of lymphocytes from humans screened for possessing anti-B box antibodies or from naïve libraries (Office Action, pages 6-7).

The Examiner asserts that the claimed invention differs from the '410 Publication by the recitation that the agent is infliximab or etanercept (Office Action, page 7). The Examiner is of the opinion, however, that the addition of the teachings of the '321 Patent would provide one of ordinary skill in the art with the requisite suggestion and reasonable expectation of success needed to establish prima facie obviousness. Once again, this is simply not the case. As explained above, in order to establish prima facie obviousness, the prior art must teach or suggest the claimed invention and provide a reasonable expectation of success. In contrast to the Examiner's assertion, the cited references do not provide the requisite suggestion and reasonable expectation of success required to establish prima facie obviousness.

The teachings of the '321 Patent are detailed above. Unlike Applicant's specification, the '321 Patent is not even directed towards HMG or its involvement in proinflammatory cytokine release. Instead the '321 Patent focuses on the use of chemical compounds, not antibodies, for the treatment of inflammatory disease. It does not provide any suggestion of combining a TNF antagonist, such as infliximab or etanercept, with an antibody that binds to an HMGB polypeptide to treat inflammatory disease. In the absence of such teachings, the person of ordinary skill in the art would not have been motivated to treat a condition in a patient characterized by activation of an inflammatory cytokine cascade which comprises administering to a patient a composition comprising an antibody that can bind to an HMGB polypeptide consisting essentially of an amino acid sequence selected from the group consisting of SEQ ID NO:1, SEQ ID NO:5, and SEQ ID NO:23 and an agent that inhibits TNF biological activity, selected from the group consisting of infliximab, etanercept, adalimumab, CDP870, CDP571, lenercept, and thalidomide.

Thus, the cited references fail to provide the suggestion and reasonable expectation of success, which are required to establish prima facie obviousness. Accordingly, reconsideration and withdrawal of the rejection are respectfully requested.

Paragraph 13. Rejection of Claims 23-42 Under 35 U.S.C. § 103(a)

The Examiner has rejected Claims 23-42 under 35 U.S.C. § 103(a) as being unpatentable over U.S. Patent No. 6,448,223 (Tracey *et al.*, hereinafter the '223 Patent) in view of the '321 Patent.

The Examiner asserts that the '223 Patent teaches a method for treating a condition characterized by activation of the inflammatory cytokine cascade, comprising administering an effective amount of an antibody that specifically binds an HMG1 protein, wherein said antibody inhibits HMG1-mediated activation of the inflammatory cytokine cascade, wherein the method further comprises administering a second agent in combination with the antibody that specifically binds an HMG1 protein, wherein the second agent is an antagonist of an early sepsis mediator, wherein the second agent is an antagonist of a cytokine selected from the group consisting of TNF, IL-1α, IL-1β, MIF and IL-6 and wherein the second agent is an antibody to TNF or an IL-1 receptor antagonist. The Examiner further asserts that the '223 Patent teaches a method for treating sepsis, comprising administering an effective amount of an antibody that specifically binds an HMG1 protein and inhibits HMG1-mediated activation of the inflammatory cytokine cascade, the method further comprising administering a second agent in combination with the antibody that specifically binds an HMG1 protein, wherein the second agent is an antagonist of an early sepsis mediator, wherein the early sepsis mediator is selected from the group consisting of TNF, IL-1α, IL-1β, MIF and IL-6, wherein the second agent is an antibody to TNF or MIF, or is an IL-1 receptor antagonist. The Examiner also asserts that the '223 Patent further teaches that the neutralizing antibodies against HMG1 are preferred for therapeutic applications, including polyclonal, monoclonal, chimeric, single-chain, and various human or humanized types of antibodies, as well as various fragments thereof such as Fab fragments and fragments produced from specialized expression systems (Office Action, pages 7-8).

The Examiner asserts that the claimed invention differs from the '321 Patent by the recitation that the agent is infliximab or etanercept (Office Action, page 8). The Examiner is of the opinion, however, that the addition of the teachings of the '321 Patent would provide one of ordinary skill in the art with the requisite suggestion and reasonable expectation of success needed to establish prima facie obviousness. Again, this is simply not the case. As explained above, in order to establish prima facie obviousness, the prior art must teach or suggest the

claimed invention and provide a reasonable expectation of success. In contrast to the Examiner's assertion, the cited references do not provide the requisite suggestion and reasonable expectation of success required to establish prima facie obviousness.

The teachings of the '321 Patent are outlined above. Unlike Applicant's specification, the '321 Patent is not even directed towards HMG or its involvement in proinflammatory cytokine release. Instead the '321 Patent focuses on the use of chemical compounds, not antibodies, for the treatment of inflammatory disease. It does not provide any suggestion of combining a TNF antagonist, such as infliximab or etanercept, with an antibody that binds to an HMGB polypeptide to treat inflammatory disease. In the absence of such teachings, the person of ordinary skill in the art would not have been motivated to treat a condition in a patient characterized by activation of an inflammatory cytokine cascade which comprises administering to a patient a composition comprising an antibody that can bind to an HMGB polypeptide consisting essentially of an amino acid sequence selected from the group consisting of SEQ ID NO:1, SEQ ID NO:5, and SEQ ID NO:23 and an agent that inhibits TNF biological activity, selected from the group consisting of infliximab, etanercept, adalimumab, CDP870, CDP571, lenercept, and thalidomide.

Thus, the cited references fail to provide the suggestion and reasonable expectation of success, which are required to establish prima facie obviousness. Accordingly, reconsideration and withdrawal of the rejection are respectfully requested.

Paragraph 14. Rejection of Claims 23-42 Under 35 U.S.C. § 103(a)

The Examiner has rejected Claims 23-42 under 35 U.S.C. § 103(a) as being unpatentable over Wang *et al.* (Science, *285*(5425):248-251 (1999)) in view of the '223 Patent and the '321 Patent.

The Examiner asserts that Wang *et al.* teach that HMG-1 is a late mediator of endotoxin lethality in mice, an animal model of human sepsis. The Examiner further asserts that Wang *et al.* teach that endotoxin stimulates macrophages to release large quantities of TNF and IL-1, which can precipitate tissue injury and lethal shock (endotoxemia). According to the Examiner delayed administration of antibodies to HMG-1 attenuated endotoxin lethality in mice, and administration of HMG-1 itself was lethal. Septic patients who succumbed to infection had

increased serum HMG-1 levels, suggesting that this protein warrants investigation as a therapeutic target. The Examiner also asserts that Wang *et al.* teach that recombinant rat HMG-1 was used to generate polyclonal antibodies and administration of anti-HMG-1 in two does increased the survival rate of the mice to 30%, with three does of antiserum, 70% of the mice survived, as compared with 0% survival in controls treated with three matched doses of preimmune serum. The Examiner asserts that Wang *et al.* teach that macrophages release HMG-1 when exposed to the early, acute cytokines, indicating that HMG-1 is also positioned as a mediator of other inflammatory conditions associated with increased levels of TNF and IL-1, concluding that the observations that HMG-1 itself is toxic, and that anti-HMG-1 prevents LPS lethality, point to HMG-1 as a potential target for therapeutic intervention (Office Action, page 9).

Applicant respectfully disagrees. Wang *et al.* do not teach a method of treating a condition in a patient comprising inter alia, treating with an agent that inhibits TNF biological activity, selected from the group consisting of infliximab, etanercept, adalimumab, CDP870, CDP571, lenercept, and thalidomide.

The Examiner asserts that the claimed invention differs from Wang *et al.* by the recitation that the agent is infliximab or etanercept in Claim 23 and the antibodies recited in Claims 37-42 (Office Action, page 9). The Examiner is of the opinion, however, that it would have been obvious to one skilled in the art at the time the invention was made to combine the infliximab or etanercept taught by the '321 Patent with the anti-HMG1 antibody taught by Wang *et al.* in a method of treating a condition in a patient characterized by activation of an inflammatory cytokine cascade and further to use a human, humanized, chimeric, single chain, or Fab fragment antibody taught by the '223 Patent. Furthermore, the Examiner asserts that one of ordinary skill in the art at the time the invention was made would have been motivated to do so because such TNF inhibitors shown to be effective for short term treatment of inflammation, such as rheumatoid arthritis, as taught by the '321 Patent and to use a human, humanized, chimeric, single-chain or Fab fragment antibody because they have low immunogenicity in humans. This is simply not the case. As explained above, in order to establish prima facie obviousness, the prior art must teach or suggest the claimed invention and provide a reasonable expectation of

success. In contrast to the Examiner's assertion, the cited references do not provide the requisite suggestion and reasonable expectation of success required to establish prima facie obviousness.

The teachings of the '223 and '321 Patents are outlined above. Unlike Applicant's specification, the '321 Patent is not even directed towards HMG or its involvement in proinflammatory cytokine release. Instead the '321 Patent focuses on the use of chemical compounds, not antibodies, for the treatment of inflammatory disease. It does not provide any suggestion of combining a TNF antagonist, such as infliximab or etanercept, with an antibody that binds to an HMGB polypeptide to treat inflammatory disease. In the absence of such teachings, the person of ordinary skill in the art would not have been motivated to treat a condition in a patient characterized by activation of an inflammatory cytokine cascade which comprises administering to a patient a composition comprising an antibody that can bind to an HMGB polypeptide consisting essentially of an amino acid sequence selected from the group consisting of SEQ ID NO:1, SEQ ID NO:5, and SEQ ID NO:23 and an agent that inhibits TNF biological activity, selected from the group consisting of infliximab, etanercept, adalimumab, CDP870, CDP571, lenercept, and thalidomide.

Thus, the cited references fail to provide the suggestion and reasonable expectation of success, which are required to establish prima facie obviousness. Accordingly, reconsideration and withdrawal of the rejection are respectfully requested.

Information Disclosure Statement

An Information Disclosure Statement (IDS) was filed on May 8, 2006. Review and entry of the IDS is respectfully requested.

CONCLUSION

In view of the above amendments and remarks, it is believed that all claims are in condition for allowance, and it is respectfully requested that the application be passed to issue. If the Examiner feels that a telephone conference would expedite prosecution of this case, the Examiner is invited to call the undersigned.

Respectfully submitted,

HAMILTON, BROOK, SMITH & REYNOLDS, P.C.

By Kristin Connarn

Kristin A. Connarn
Registration No. 57,025
Telephone: (978) 341-0036
Facsimile: (978) 341-0136

Concord, MA 01742-9133
Dated: August 21, 2006